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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,522	09/28/2001	Thomas Krahn	100717-502 / Bayer 10139	5606

27384 7590 10/08/2008
NORRIS, MCLAUGHLIN & MARCUS, PA
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NEW YORK, NY 10022

EXAMINER

DO, PENSEE T

ART UNIT	PAPER NUMBER
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1641

MAIL DATE	DELIVERY MODE
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10/08/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/966,522	KRAHN ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6-43 is/are pending in the application.
- 4a) Of the above claim(s) 6-16 and 24-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-23 and 43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 6-43 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/27/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Finality Withdrawn

As an outcome of the Pre-Brief Conference requested by Applicants on April 18, 2008, the prosecution of this application is withdrawn.

Withdrawn Rejection(s)

Rejection under 103 is withdrawn herein.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 17 is amended to recite "the fluorescent dye is in a form that permits the fluorescent dye to permeate the membrane". However, the specification fails to support such "form" that permits the fluorescent dye to permeate the membrane. The specification only describes fluorescent dye such as bis(1,3-dibutylbarbituric acid) trimethanexonol (Dibac4(3)) and a masking dye used is brilliant Black on page 8. The specification fails to teach any modification of such dyes into a form that permeate the cell membrane. As taught by Walt (US 6,210,910),

Art Unit: 1641

impermeant cells can be conjugated to acetoxymethyl ester to allow uptake by cells.(see col. 15, lines 46-47).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 17-21, 23 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roth et al. (US 5,545,535 filed on November 1, 1993) in view of Wan et al. (Journal of Immunological Methods 162 (1993) pp. 1-7) and further in view of Cubbage (US 5,582,982).

Roth teaches using four different fluorescent dyes to label bacteria. One of the dyes is a fluorescent dye that is highly membrane-permeant cyanide dye derivatives and labels all bacteria and stains the nucleic acid of the bacterial cell. (see abstract, dye formula I; col. 6, line 55-col. 13, line 28).

However, Roth fails to teach a masking dye in a solution to reduce non-specific background light emitted from said solution by at least 10%, 30%, 50% or 70% compared to the non-specific background light emitted from said solution in the absence of said masking dye.

Wan teaches a method of using fluorescein conjugated E.Coli particles and second dye such as Trypan blue to quench the extracellular fluorescence in the solution. That means Trypan blue absorbs and the extracellular fluorescence which

Art Unit: 1641

cause the solution to emit non-specific background light in the solution while the fluorescent that absorbs into the cells are being measured. Quenching the extracellular fluorescence thus means reducing non-specific background light in solution. (see abstract, page 3 "Phagocytosis assay" and "results"). Trypan blue is obviously impermeant to the membrane of the cell because it quenches extracellular fluorescence. Wan also teaches that the concentration of trypan blue require to completely quench extracellular fluorescence was determined by exposing $3 \text{ or } 6 \times 10^8$ particles/well to serial dilutions of the dye in a 96-well plate. Complete quenching of the fluorescence was obtained with 250 ug/ml of the dye. Thus, Wan meets the requirement that the non-specific background in solution is reduced by at least 30%, 50% and 70% (claims 18-20). Since trypan blue can quench or reduce non-specific background, it would be able to perform functions such as to improve the signal to noise ratio by at least 300%.

It would have been obvious to one of ordinary skills in the art to use an extra dye such Tryptan blue as taught in Wan to quench extracellular fluorescence in the method of Roth because Roth uses a combination of four fluorescent dyes to stain cells and thus there would be plenty of extracellular fluorescence which would cause non-specific background light, and Tryptan blue can completely quench extracellular fluorescence.

However, Roth and Wan fail to teach a kit.

Cubbage teaches a kit comprising a fluorescent probe and a background-reducing compound that diffuses into and onto the biological entity. (see col. 2, line 45-col. 7, line 27).

It would have been obvious to one of ordinary skills in the art package the components taught by Roth and Wan into a kit as taught by Cubbage to the advantage of economical convenience and storage.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Roth in view of Wan et al. (Journal of Immunological Methods 162 (1993) pp. 1-7), and further in view of Cubbage et al. (US 5,582,982) as applied to claim 17-21, 23 above, and further in view of Van Aken (US 5,489,537).

Roth, Wan and Cubbage have been discussed above.

However, Roth, Wan and Cubbage fails to teach Brilliant Black as a fluorescent dye.

Van Aken teaches a method and kit for determining the presence or absence of a substance by detection of a colloidal dye associated with agglutinated particles. The colloidal dye is a background-enhancing dye, which reduces non-specific background to enhance optical detection. The background-enhancing dye is a water-soluble dye such as Brilliant Black. (see col. 21, lines 58-67).

It would have been obvious to one of ordinary skills in the art to use Brilliant Black as a masking or quenching dye in the kit for use in the method of Roth, Wan and Cubbage because these references teach using quenching or background reducing dye, which reduces background light in assay. Since Brilliant Black is known for enhancing the background in an assay, which uses optical detection, it would motivate one of ordinary skills in the art to use Brilliant Black in assays such as one taught by

Art Unit: 1641

Wan and Cubbage because both Wan and Cubbage teach using fluorescent label, which is known for producing non-specific background.

Response to Arguments

Applicant's arguments with respect to claims 17-23, 43 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Application/Control Number: 09/966,522
Art Unit: 1641

Page 7

/Pensee T. Do/
Examiner, Art Unit 1641

/Mark L. Shibuya, Ph.D./
Supervisory Patent Examiner, Art Unit 1641